REMARKS

Status of the Claims

Claims 1-7 and 9-27 are currently pending. Claim 8 has been canceled without prejudice or disclaimer of the subject matter claimed therein. Claims 9-26 are withdrawn from consideration as being directed to a separate invention. Claims 1-7 and 27 are currently under examination.

Amendments to the Claims

Claim 1 has been amended to recite that the test subject is a human. Representative support for this amendment can be found in original claim 8.

Claim 27 has been amended to recite that the kit is directed for assessing $CD4^{lo}CD40^{hi}$ levels in humans. Representative support can be found in original claim 8.

The amendments to the claims do not introduce prohibited new matter.

Rejections under 35 U.S.C. § 102(b)

Claims 1, 4, 5, and 7 are rejected under 35 U.S.C. § 102(b) as anticipated by Wagner *et al.* (PNAS, March 19, 2002, Vol. 99, pp. 3782-3787).

The Office Action alleges that Wagner *et al.* anticipate the claimed invention because Wagner *et al.* disclose antibody staining and flow cytometry to detect CD4+CD40+ T cells. Wagner *et al.* disclose comparing two different strains of mice for predicting diabetes.

Without acquiescing to the merits of the rejection, Applicants have amended the claims to recite that the test subject is a human. Wagner *et al.* do not disclose detecting autoimmune diseases in humans. It is therefore respectfully requsted that this rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

A. Claims 2, 3, and 6 are rejected under 35 U.S.C. § 103(a) as obvious over Wagner *et al.* in view of Jeffery (Novartis Foundation Symposium, 2001, vol. 234, pp. 149-161, Abstract) and Waid *et al.* (FASEB, 2003, 17(7), p. C177).

Claims 2, 3, and 6 depend directly or indirectly from Claim 1 and include the features of

claim 1. Applicants respectfully submit that the teachings of Jeffery and Waid *et al.* do not cure the deficiencies of Wagner *et al.* Jeffery only discloses a CD4/CD8 ratio may affect regulation of IL-4 and IL-5. The Office Action alleges that the CD4/CD8 ratio speculated by Jeffery is relevant to chronic obstructive pulmonary disease. The present invention is however directed to T cells with a low expression of CD4 and a high expression of CD40. Accordingly, the ratio of Jeffery is irrelevant to the autoimmune detection methods of the claimed invention. Furthermore, Jeffery does not disclose detecting an autoimmune disease in a human by determining the levels of $CD4^{lo}$ $CD40^{hi}$ T cells.

Waid *et al.* only teach that injecting OVA and then challenging the lungs with a repeated exposure increases $CD4^{+}TCR^{+}CD40^{+}$, IL-2, IL-4, IL-10, and IFNγ levels. The response disclosed by Waid *et al.* is an immune challenge, not an autoimmune response. The Office Action relies on Waid *et al.* to disclose $CD4^{+}CD40^{+}$ T cells in asthma. The Office Action alleges that changes in $CD4^{+}CD40^{+}$ T cells in asthma correlate to the CD4/CD8 ratio speculated by Jeffery. However, chronic obstructive pulmonary disease and asthma are different diseases. Accordingly, the immune response from an immune challenge with OVA disclosed by Waid *et al.* is not equivalent to chronic obstructive pulmonary disease disclosed by Jeffery. Thus, one cannot correlate changes in CD4+CD40+ T cells in asthma as taught by Waid *et al.* with the CD4/CD8 ratio taught by Jeffery. Furthermore, Waid *et al.* does not disclose detecting an autoimmune disease in a human by determining the levels of $CD4^{lo}$ $CD40^{hi}$ T cells.

Accordingly, neither Jeffery nor Waid *et al.* provide a method for determining if a subject has an auto-immune disease by comparing $CD4^{lo}CD40^{hi}$ T cell levels to a control. Neither Waid *et al.* nor Jeffery disclose the missing elements or provide a reason to modify the teachings of Wagner *et al.* to arrive at the claimed invention. Consequently, the combination of the cited references does not render the claimed invention obvious. It is therefore respectfully requested that this rejection be withdrawn.

B. Claim 27 is rejected under 103(a) as obvious over Wagner *et al.* in view of Foster *et al.* (US Patent 4,444,879).

The deficiencies of Wagner *et al.* are discussed above. Foster *et al.* are relied upon for disclosing kits, but Foster *et al.* do not cure the deficiencies of Wagner *et al.* Foster *et al.* do not

teach or suggest a kit for detecting autoimmune disease in a human.

Accordingly, there is no reason to combine the teachings of Wagner *et al.* with Foster *et al.* and to make the necessary changes to obtain the kit recited in the present claim with reasonable expectation of success. Therefore, the combination of the cited references does not render the claimed invention obvious and it is respectfully requested that this rejection be withdrawn.

Double Patenting

Claims 1, 4, 5, 7, 8, and 27 are provisionally rejected on the ground of obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application 10/399,384 ('384).

The Office Action alleges that the claims are directed to methods that are not patentably distinct from each other. The present application is a national phase application of international application PCT/US04/21646, filed on July 7, 2004. Application '384 was filed on April 7, 2006, as a continuation-in-part application of the present application. The present application with claims directed to the genus has an earlier filing date than Application '384 with claims directed to the species. Accordingly, the present application cannot be obvious over Application '384.

Claims 2, 3, and 6 are provisionally rejected on the ground of nonstatutory obviousness type double patenting as being unpatentable over claims 1-13 of copending Application No. 11/399,384 ('384) in view of Jeffery and Waid *et al.*

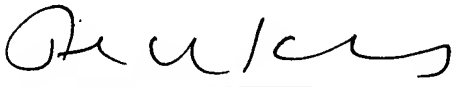
As discussed above, the present application is senior to the '384 Application. Further, Application '384 is directed to determining whether a subject has type I or type II diabetes. Jeffery and Waid *et al.* are not directed to determining whether a subject has type I or type II diabetes. Also as discussed above, neither Jeffery nor Wald *et al.* teach a method for determining if a human subject has an autoimmune disease by comparing $CD4^{lo}CD40^{hi}$ levels to a control. Accordingly, there is no motivation to combine the teachings of the cited references and to obtain the claimed invention. Thus, Application '384 and the cited references do not render the claimed invention obvious.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, she is invited to telephone the undersigned at their convenience.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
Morgan, Lewis & Bockius LLP



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